

EAGOT
Cervical Cancer Committee

**Discussion about clinical trials or situation of
the chemotherapies and/or ICI in each country**



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From a survey on ***Apr 2022***

Current Status of Cervical Cancer(CC) Treatment Strategy in Each Country **Q1 ; Indication for Surgery**

Q1 ; Which FIGO stage of CC do you (or your country) consider appropriate for Radical Hysterectomy (RH) ?

A1 ; Please choice suitable FIGO stage for RH;

(FIGO2018)

IA1 · IA2

IB1 · IB2 · IB3

IIA1 · IIA2 · IIB

IIIA · IIIB · IIIC1r · IIIC2r

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(FIGO2018)

IA1 · IA2

IB1 · IB2 · IB3

IIA1 · IIA2 · IIB

IIIA · IIIB · IIIC1r · IIIC2r

KGOG1	KGOG2	TGOG	CGCS	JGOG
	IA1	IA1	IA1	
IA2	IA2	IA2	IA2	IA2
IB1	IB1	IB1	IB1	IB1
IB2	IB2	IB2	IB2	IB2
				IB3
IIA1			IIA1	IIA1
IIA2				IIA2
				IIB
				IIIC1r

KGOG, CGCS, JGOG may choice RH for (a part of) stage II/III

Current Status of Cervical Cancer(CC) Treatment Strategy in Each Country **Q2 ; Surgical Approach and Pt. selection**

Q2-2 ; Which **surgical approach is most often used for RH?**

A2-1 ; Please choice approach;

1. Laparotomy
2. Laparoscopic
3. Robotic

Current Status of Cervical Cancer(CC) Treatment Strategy in Each Country **Q2 ; Surgical Approach and Pt. selection**

Q2-2 ; Which **surgical approach** is most often used for RH?

A2-1 ; Please choice approach;

1. Laparotomy
2. Laparoscopic
3. Robotic

KGOG1	KGOG2	TGOG	CGCS	JGOG
1	2	1	1	1
	3			2

MIS is often chosen, especially in Korea.

Current Status of Cervical Cancer(CC) Treatment Strategy in Each Country **Q2 ; Surgical Approach and Pt. selection**

Q2-3 ; Do you treat your patients with **NAC before RH ?**

A2-3 ; Please choice;

1. Yes
2. No

Current Status of Cervical Cancer(CC) Treatment Strategy in Each Country **Q2 ; Surgical Approach and Pt. selection**

Q2-3 ; Do you treat your patients with NAC before RH ?

A2-3 ; Please choice;

1. Yes
2. No

KGOG1	KGOG2	TGOG	CGCS	JGOG
2	2	1	2	2

Only TGOG use NAC in practice
(in clinical trial at Taiwan)

Current Status of Cervical Cancer(CC)Treatment Strategy in Each Country **Q3 ; Adjuvant Therapy**

Q3-1 ; What **adjuvant therapies are often used after RH ?**

A3-1 ; Please choice;

1. (Chemo)Radiotherapy
2. Chemotherapy

Current Status of Cervical Cancer(CC) Treatment Strategy in Each Country **Q3 ; Adjuvant Therapy**

Q3-1 ; What **adjuvant therapies are often used after RH ?**

A3-1 ; Please choice;

1. (Chemo)Radiotherapy
2. Chemotherapy

KGOG1	KGOG2	TGOG	CGCS	JGOG
1	1	1	1	1
		2		2

In Taiwan and Japan, chemotherapy appears to be an option for postoperative treatment.

Current Status of Cervical Cancer(CC)Treatment Strategy in Each Country **Q4 ; Chemo Agents**

Q4 ; Which chemotherapeutic agents are covered by insurance for the treatment of CC pts. in your country?

A4 ; Please choice drugs;

1. Cisplatin
2. Carboplatin
3. Nedaplatin
4. Paclitaxel
5. Docetaxel
6. Irinotecan
7. Topotecan
8. Gemcitabine
9. Bevacizumab
10. Pembrolizumab
11. Others

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11. Others

KGOG1	KGOG2	TGOG	CGCS	JGOG
1	1	1	1	1
2	2	2	2	2
	3			3
4	4	4	4	4
	5			
	6	7		6
7	7			7
	8			
9	9	9		9

TGOG;
4 · 9 Only for rec.

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11. Others

	KGOG1	KGOG2	TGOG	CGCS	JGOG
1	1	1	1	1	1
2	2	2	2	2	2
3	3	3	3	3	3
4	4	4	4	4	4
5	5	5	5	5	5
6	6	6	6	6	6
7	7	7	7	7	7
8	8	8	8	8	8
9	9	9	9	9	9

At Apr 2022

TGOG;
4 · 9 Only for rec.

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- 11. Others**

	KGOG1	KGOG2	TGOG	CGCS	JGOG
1	1	1	1	1	1
2	2	2	2	2	2
3		3			3
4	4	4	4	4	4
5		5			
6		6			6
7		7			7
8		8			
9		9	9		9
10?		10?	10?	10?	10?
11?					11?

At Apr 2022

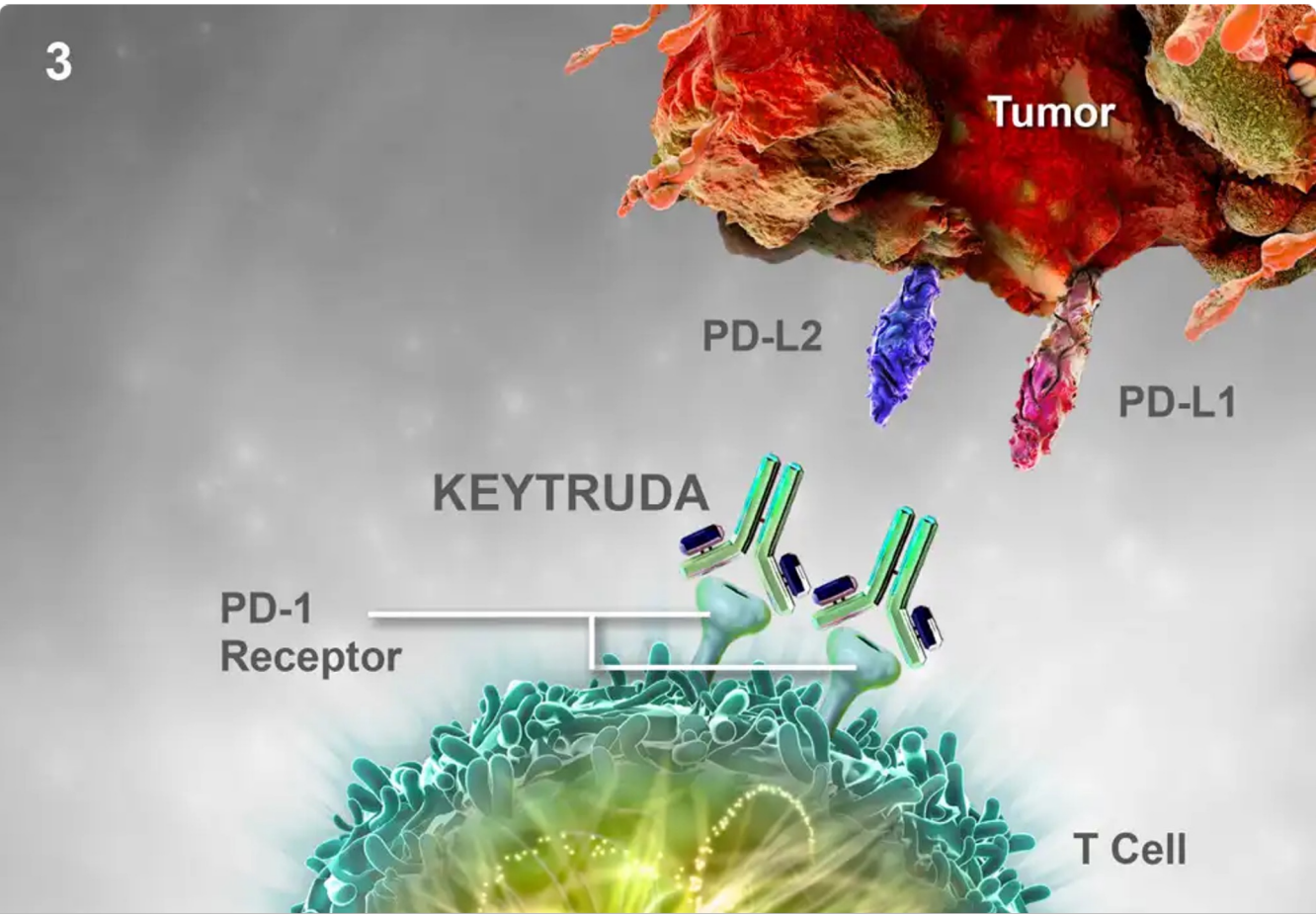
TGOG;
4 · 9 Only for rec.



DISCUSSION

DISCUSSION (1)

3



DISCUSSION (1)

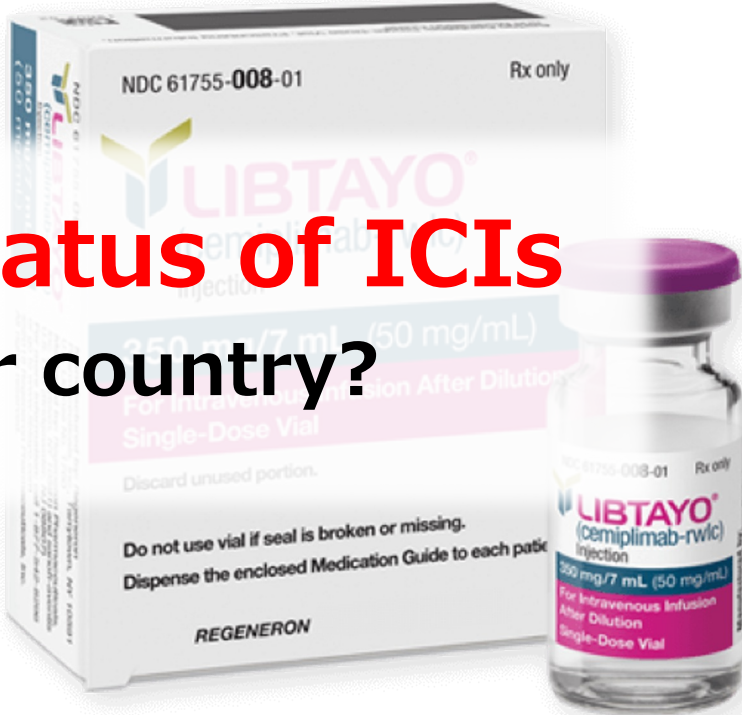
3

What is the **approval status of ICIs** for cervical cancer in your country?

PD-1 Receptor

Tumor

T Cell



DISCUSSION (1)

3

What is the approval status of ICIs for cervical cancer in your country?

1. Neo-adjuvant
2. Locally advanced
3. r/m chemo-naïve (1st line)
4. r/m chemo-resistant (2nd line or later)

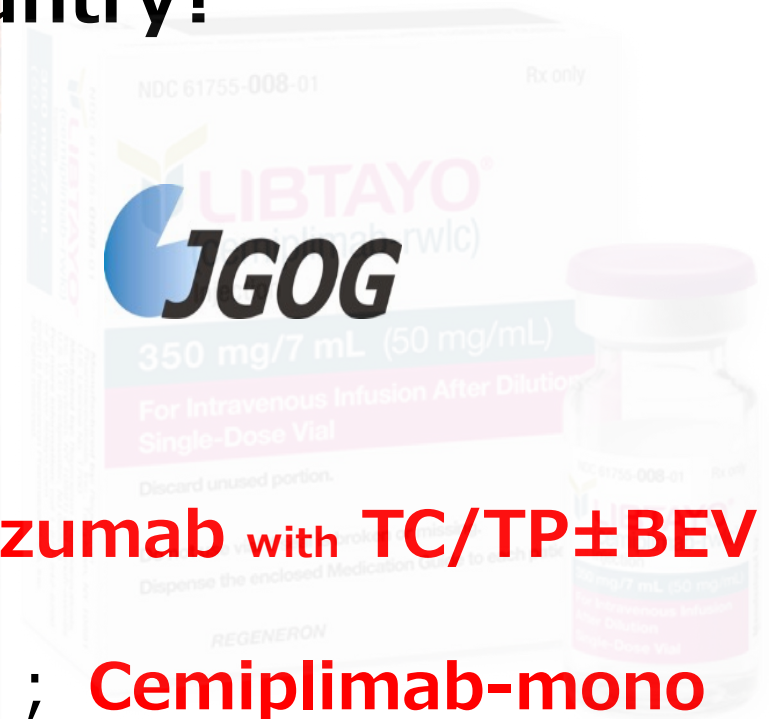


DISCUSSION (1)

3

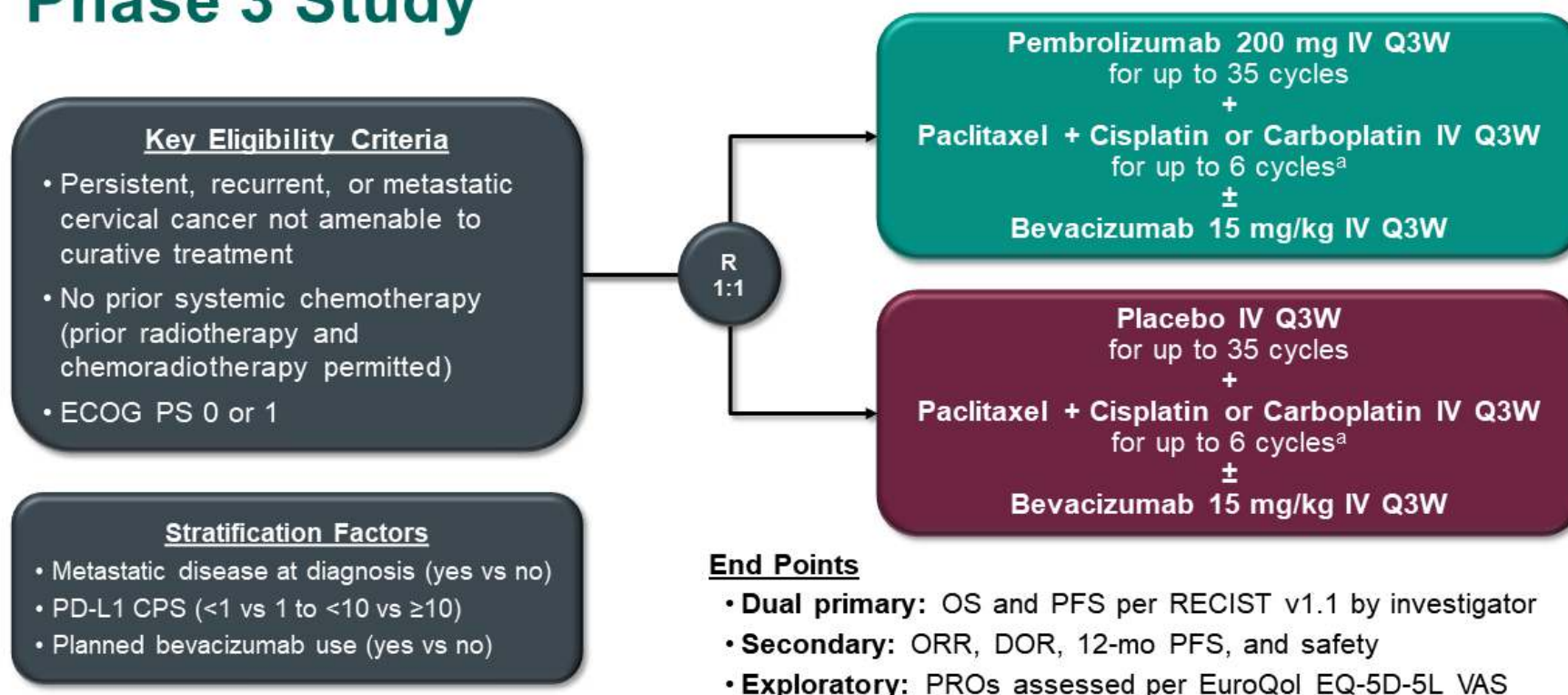
What is the approval status of ICIs for cervical cancer in your country?

1. Neo-adjuvant
2. Locally advanced
3. r/m chemo-naïve (1st line) ; **Pembrolizumab with TC/TP±BEV**
4. r/m chemo-resistant (2nd line or later) ; **Cemiplimab-mono**



KEYNOTE-826 ; Pembrolizumab + chemotherapy for r/m cervical cancer (chemo-naïve)

KEYNOTE-826: Randomized, Double-Blind, Phase 3 Study



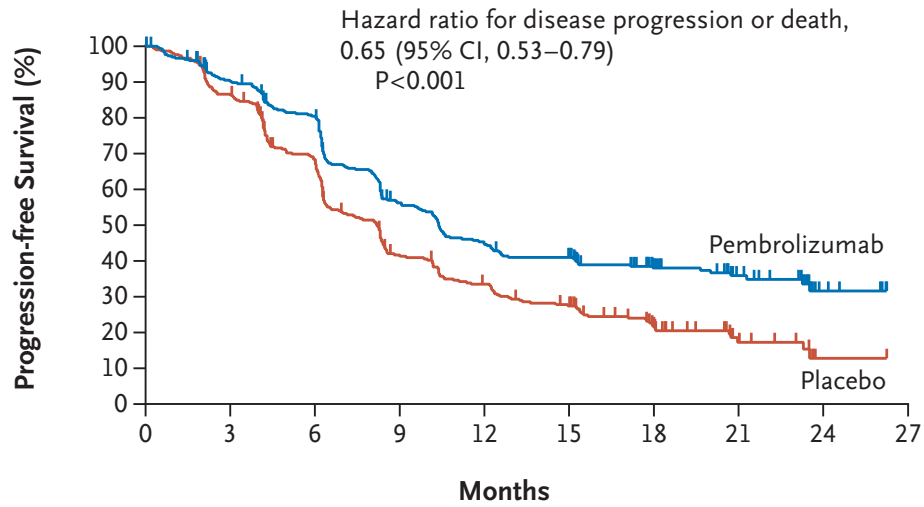
^aPaclitaxel: 175 mg/m². Cisplatin: cisplatin 50 mg/m². Carboplatin: AUC 5 mg/mL/min. The 6-cycle limit was introduced with protocol amendment 2, although participants with ongoing clinical benefit who were tolerating chemotherapy could continue beyond 6 cycles after sponsor consultation.

CPS, combined positive score (number of PD-L1-staining cells [tumor cells, lymphocytes, macrophages] divided by the total number of viable tumor cells, multiplied by 100); PROs, patient-reported outcomes; VAS, visual analog scale. KEYNOTE-826 ClinicalTrials.gov identifier, NCT03635567.

PFS

OS

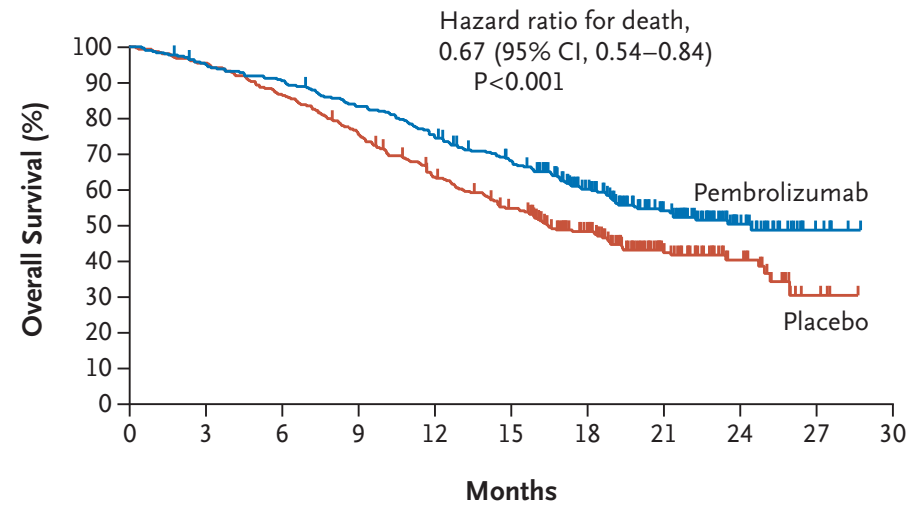
B Intention-to-Treat Population



No. at Risk

Pembrolizumab	308	263	229	155	123	110	70	35	10	0
Placebo	309	259	195	113	89	71	39	13	1	0

B Intention-to-Treat Population

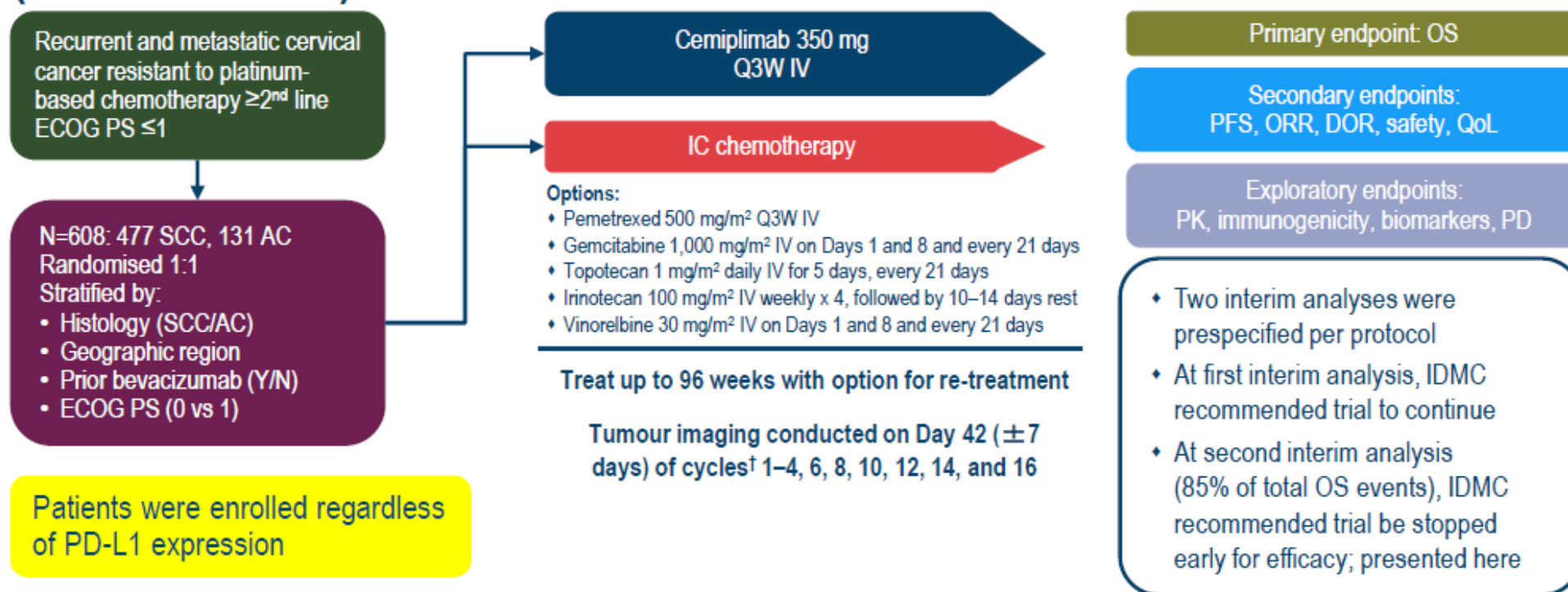


No. at Risk

Pembrolizumab	308	291	277	254	228	201	145	89	36	6	0
Placebo	309	295	268	234	191	160	116	60	28	4	0

EMPOWER-CERVICAL1 ; Cemiplimab-mono for r/m cervical cancer (chemo-resistant)

EMPOWER-CERVICAL 1/GOG-3016/ENGOT-CX9 STUDY DESIGN* (NCT03257267)

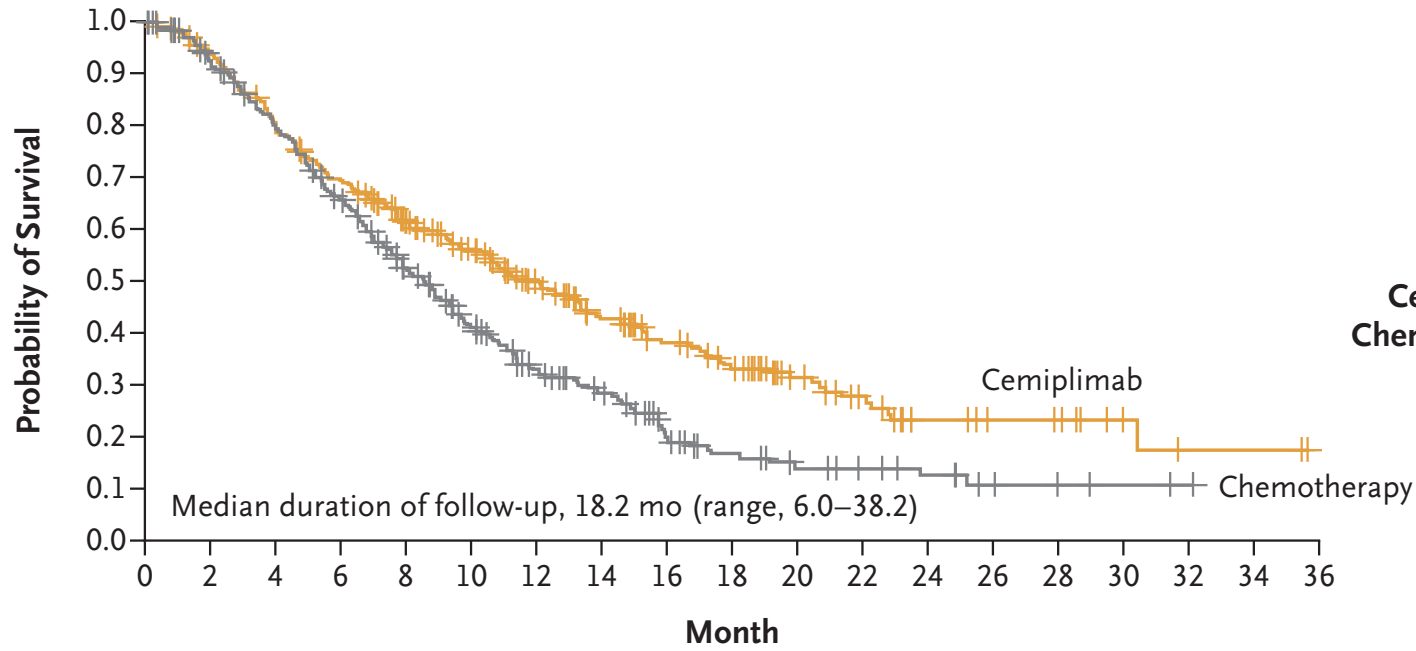


*Performed according to ENGOT Model C.^{††}To account for differences in drug administration schedules, one cycle is defined as 6 weeks.

AC, adenocarcinoma or adenosquamous carcinoma; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IC, investigator's choice; IDMC, Independent Data Monitoring Committee; IV, intravenously; ORR, objective response rate; OS, overall survival; PD, pharmacodynamics; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; PK, pharmacokinetics; Q3W, every 3 weeks; QoL, quality of life; SCC, squamous cell carcinoma.

1. Vergote I et al. *Int J Gynecol Cancer*. 2019;0:1–4.

A Overall Survival, All Patients



	No. of Patients	Median Overall Survival (95% CI) <i>mo</i>
Cemiplimab	304	12.0 (10.3–13.5)
Chemotherapy	304	8.5 (7.5–9.6)
Hazard ratio for death, 0.69 (95% CI, 0.56–0.84)		
Two-sided P<0.001		

No. at Risk

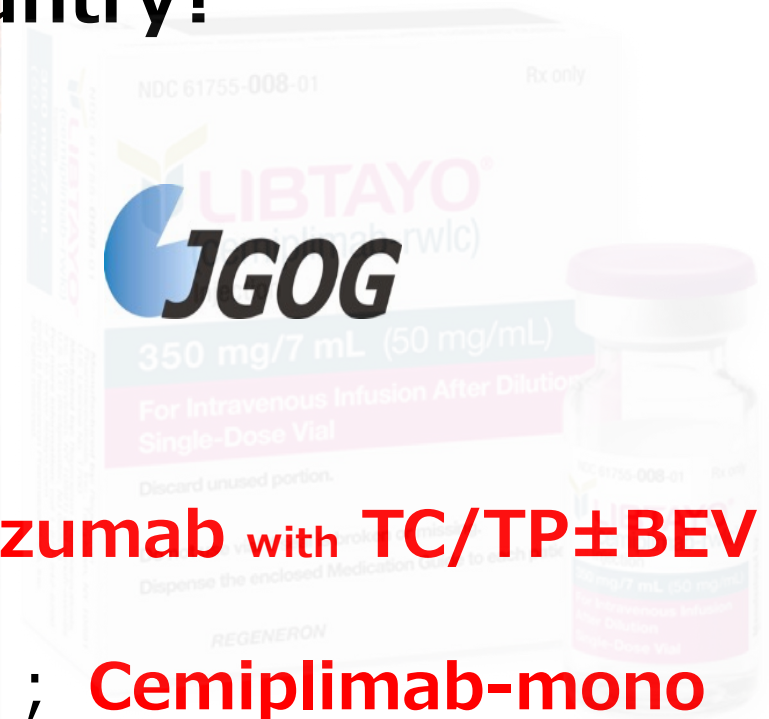
Cemiplimab	304	281	236	206	167	139	110	83	65	52	35	26	13	10	9	4	2	2	0
Chemotherapy	304	264	224	183	132	99	70	54	32	22	15	12	9	5	3	2	1	0	0

DISCUSSION (1)

3

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4. r/m chemo-resistant (2nd line or later) ; **Cemiplimab-mono**



DISCUSSION (1)

3

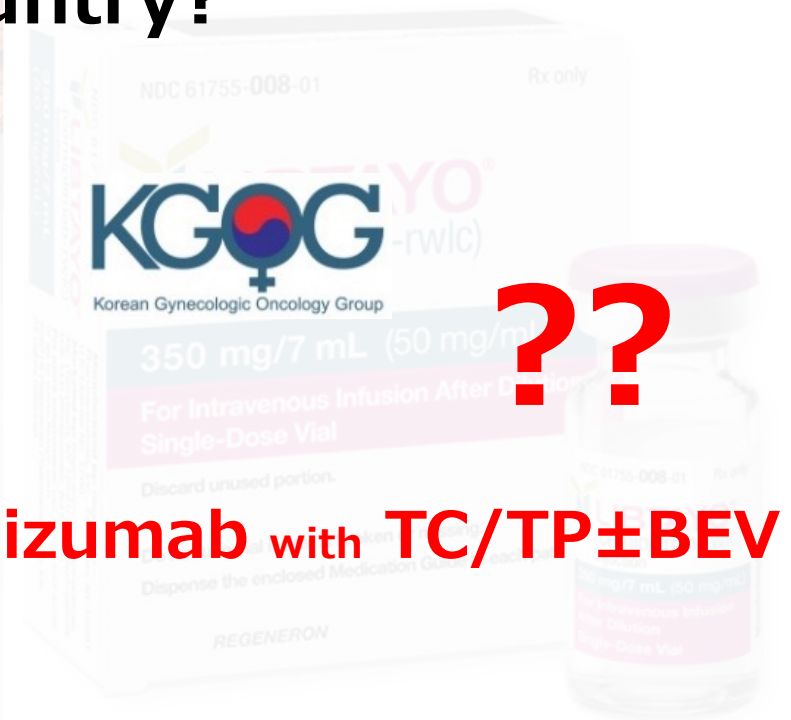
What is the approval status of ICIs for cervical cancer in your country?

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2. Locally advanced

3. r/m chemo-naïve (1st line) ; **(CPS \geq 1) Pembrolizumab with TC/TP \pm BEV**

4. r/m chemo-resistant (2nd line or later)



DISCUSSION (1)

3

What is the approval status of ICIs for cervical cancer in your country?

1. Neo-adjuvant

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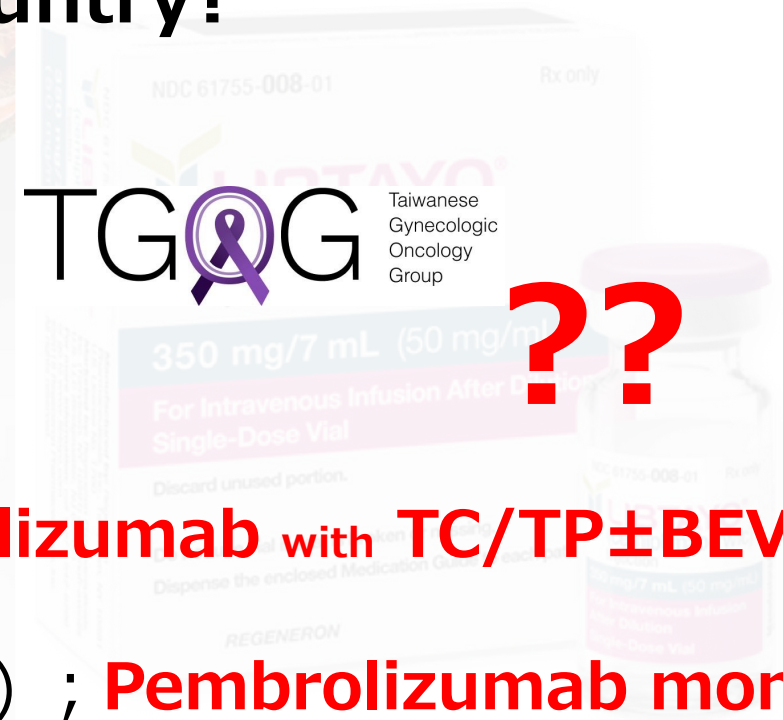
3. r/m chemo-naïve (1st line) ; **Pembrolizumab** with **TC/TP±BEV**

4. r/m chemo-resistant (2nd line or later) ; **Pembrolizumab mono**

(CPS \geq 1)

TGOG Taiwanese Gynecologic Oncology Group

??



DISCUSSION (1)

3

What is the approval status of ICIs for cervical cancer in your country?

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??



DISCUSSION (2)

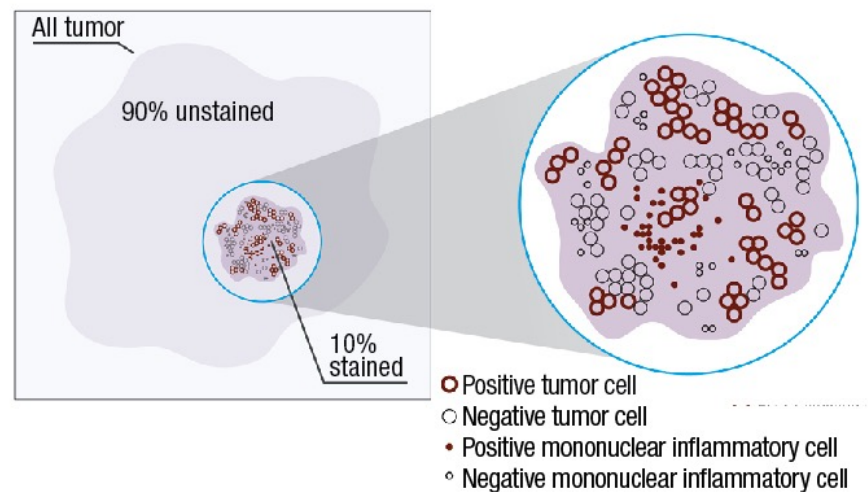
Is it necessary to check

■ **PD-L1 status**

■ **CPS ; Combined positive score**

when using ICIs for cervical cancer in your country?

**Fig. 6. CPS: Example calculation method
tumor area with staining**



In the stained area, 50 of 100 tumor cells are PD-L1 positive, and there are 34 PD-L1-positive mononuclear inflammatory cells (MIC).

Combined positive score:

$$\frac{84 \text{ positive cells}}{100 \text{ tumor cells}} \times 100 \cong 84$$

10% of 84 = 8

Specimen is PD-L1 positive.

DISCUSSION (2)

Is it necessary to check

■ **PD-L1 status**

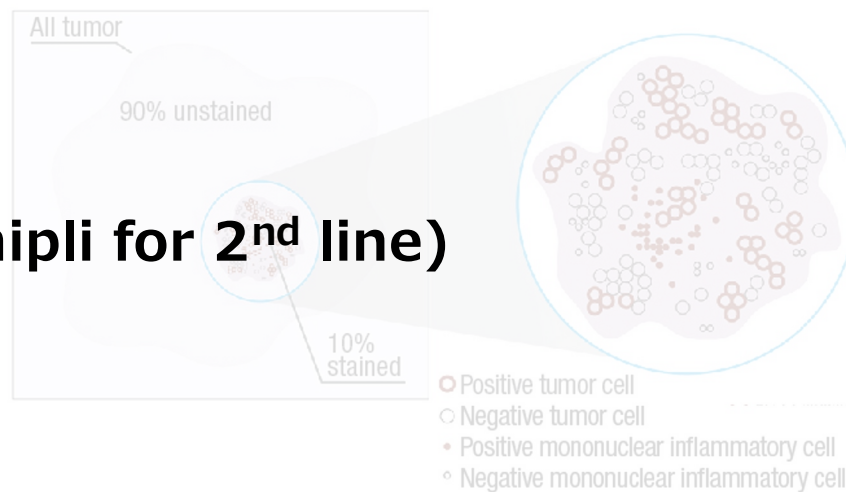
■ **CPS ; Combined positive score**

when using ICIs for cervical cancer in your country?



We can use ICIs
(pembro for 1st line, Cemipli for 2nd line)
regardless of CPS.

Fig. 6. CPS: Example calculation method
tumor area with staining



In the stained area, 50 of 100 tumor cells are PD-L1 positive, and there are 34 PD-L1-positive mononuclear inflammatory cells (MIC).

Combined positive score:

$$\frac{84 \text{ positive cells}}{100 \text{ tumor cells}} \times 100 \cong 80$$

10% of 80 = 8

Specimen is PD-L1 positive.

DISCUSSION (2)

Is it necessary to check

- PD-L1 status
- CPS ; Combined positive score

when using ICIs for cervical cancer in your country?



Pembro (1st line)
CPS ≥ 1

??



Pembro (1st line)
CPS ≥ 1

??



Fig. Calculation method of staining

- Positive tumor cell
- Negative tumor cell
- Positive mononuclear inflammatory cell
- Negative mononuclear inflammatory cell

??

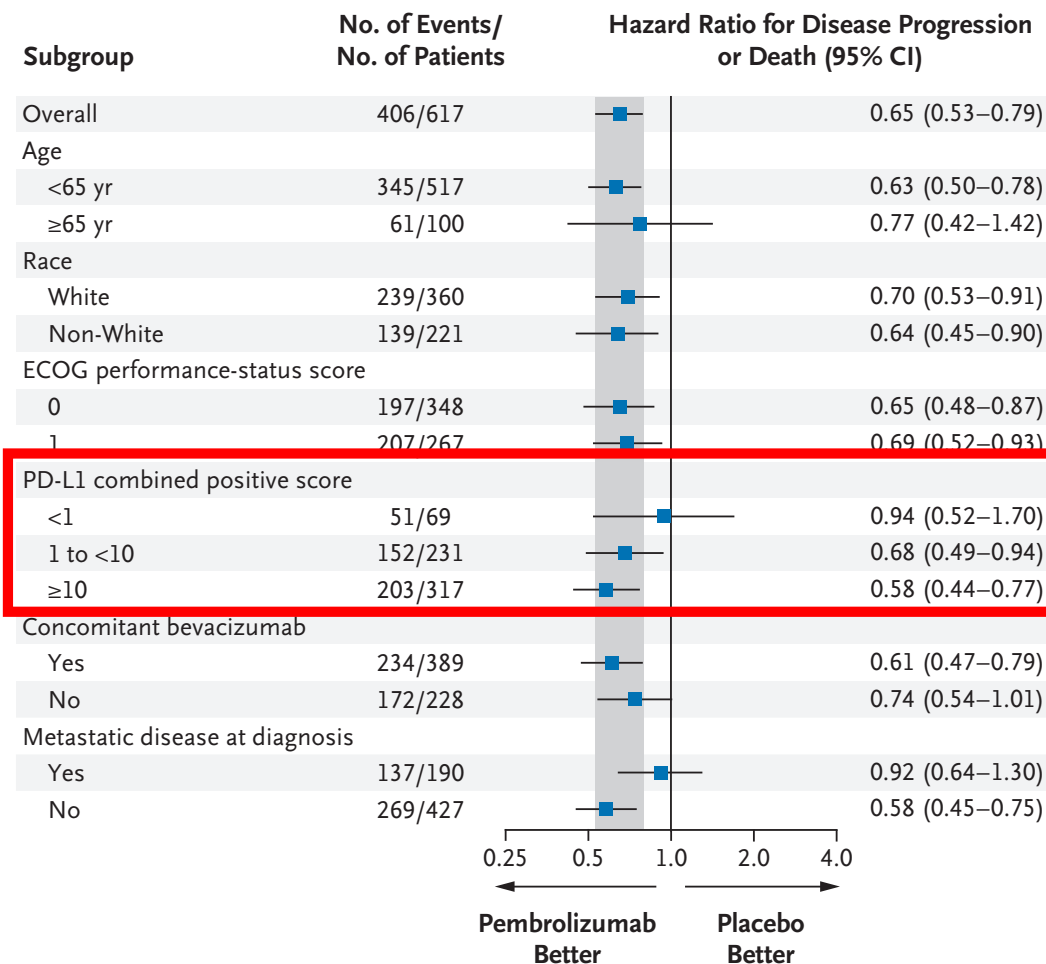


Pembro (1st line)
CPS

??

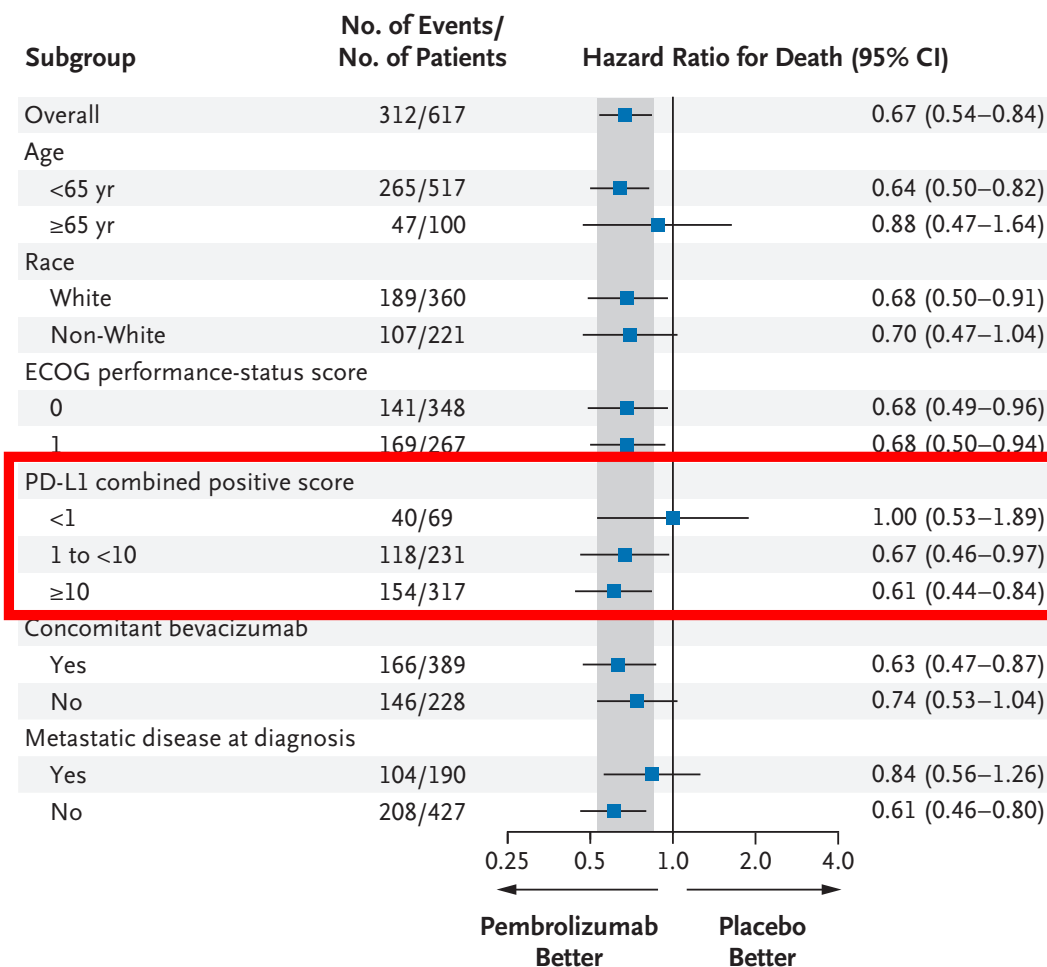
PFS

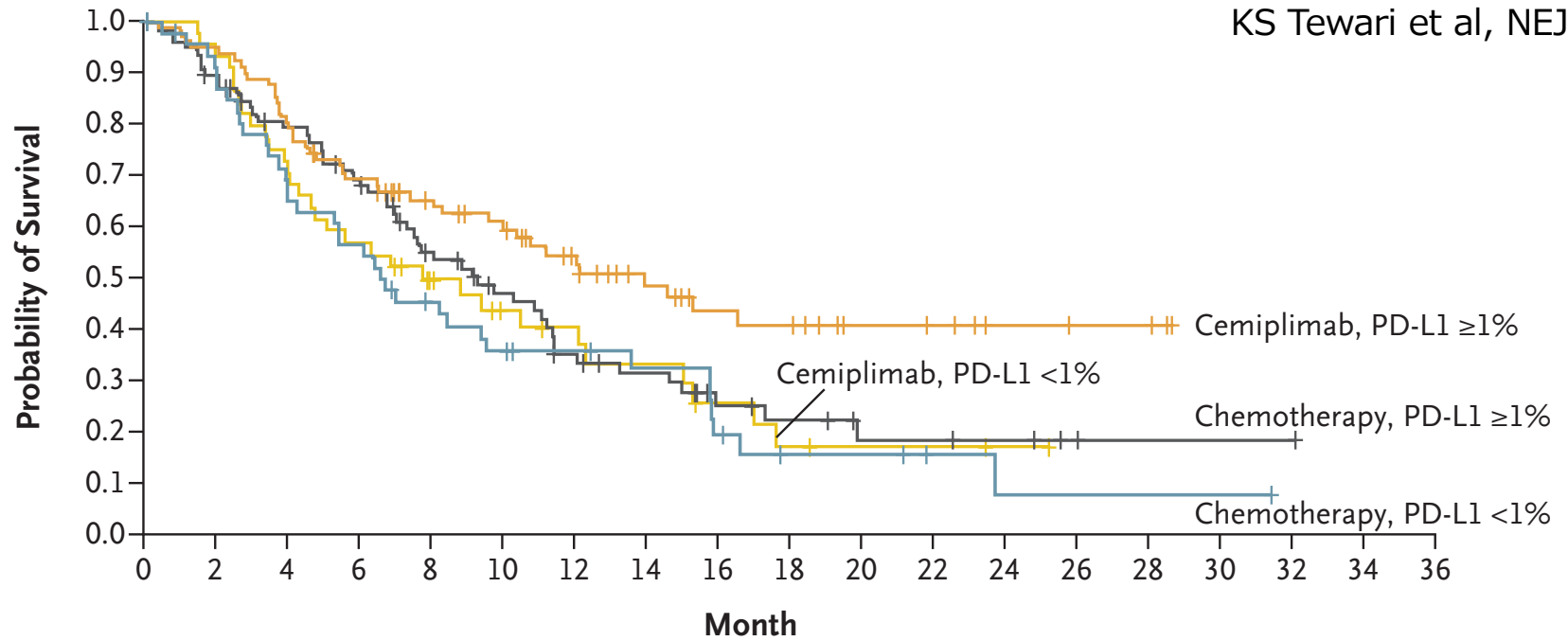
D Subgroup Analysis in Intention-to-Treat Population



OS

D Subgroup Analysis in Intention-to-Treat Population





No. at Risk

Cemiplimab, PD-L1 $\geq 1\%$	82	78	65	55	45	39	30	22	16	15	10	9	4	3	3	0	0	0	0
Cemiplimab, PD-L1 $< 1\%$	44	41	30	25	18	13	11	9	6	4	3	3	1	0	0	0	0	0	0
Chemotherapy, PD-L1 $\geq 1\%$	80	69	58	50	36	28	20	16	10	8	5	5	4	2	1	1	1	0	0
Chemotherapy, PD-L1 $< 1\%$	48	40	30	26	19	15	12	10	6	4	4	2	1	1	1	1	0	0	0

Figure 3. Overall Survival According to PD-L1 Expression Status in the Overall Trial Population.

Kaplan–Meier estimates of overall survival according to PD-L1 expression status are shown. Patients with PD-L1 expression (measured as the tumor cell expression score [the percentage of tumor cells expressing PD-L1]) of 1% or greater generally had enhancement of the overall survival benefit. Patients with PD-L1 expression of less than 1% generally had an overall survival benefit as good as or slightly better than that of patients who received chemotherapy. Tick marks indicate censored data.

DISCUSSION (3)

What is the current status of clinical trials on chemotherapy being conducted in your country?





DISCUSSION (3)

What is the current status of clinical trials on chemotherapy being conducted in your country?

Open

gynecological cancer

(KGOG1043)

ENGOT_Cx12_GOG3037: A Randomized, Open-Label, Phase 3 Trial of Tisotumab Vedotin vs Investigator's...

- PI Sungjong Lee
- Registration Date/ Last Update Posted 2022-05-10/ 2022-05-10
- Current Enrollment / Estimated Enrollment 130 / 482 (27.0%)

ENGOT_Cx12_GOG3037:

A Randomized, Open-Label, Phase 3 Trial of Tisotumab Vedotin vs Investigator's Choice Chemotherapy in Second- or Third-Line Recurrent or Metastatic Cervical Cancer



DISCUSSION (3)

What is the current status of clinical trials on chemotherapy being conducted in your country?

A Randomized trial of adjuvant chemotherapy versus chemoradiotherapy for stage IB-IIA cervical cancer after radical hysterectomy

Adjuvant Chemotherapy Versus Radiotherapy For Postoperative Cervical Cancer ; a phase 3 trial (AFTER trial)



Japanese Gynecologic Oncology Group
Cervical cancer committee
JGOG1082



DISCUSSION (3)

What is the current status of clinical trials on chemotherapy being conducted in your country?



DISCUSSION (4)

What about adding ICIs on chemoradiotherapy for locally advanced cervical cancer?

